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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/657,289	09/07/2000	Kevin P Francis	9400-0006	1639

20855 7590 02/11/2003

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/11/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/657,289

Applicant(s)

FRANCIS ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8,21,22,24-29,34-36,49,56,58,60,64 and 68-86 is/are pending in the application.

4a) Of the above claim(s) 60 and 83-86 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.

- 6) ☒ Claim(s) 1-8,21,22,24-28,34-36,49,56,58,64 and 68-82 is/are rejected.

- 7) ☒ Claim(s) 29 is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.

- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)

- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.

- 5) ☐ Notice of Informal Patent Application (PTO-152)

- 6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed November 13, 2002 canceling claim 62 and amending claims 79-82 has been entered.

Claims 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 60, 64 and 68-86 are pending.

Claims 60 and 83-86 are withdrawn. Claims 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 64 and 68-82 are under consideration.

Claim Objections

Claims 1 and 21 are objected to because of the following: the claims recite abbreviations "lux" and "luc" that should be preceded by the full names such as "luciferase gene", for example.

Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 28 recites *luxC*, *luxD* and *luxE* that are included in the scope of claim 21 from which claim 28 depends. For the purpose of the examination, claim 28 was construed as dependent from claim 22.

Appropriate correction is required.

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 79-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to replace "substrate" with "one or more substrates". Applicants indicate support for the amendment on page 23, line 22, tp page 25, line 20, and page 32, lines 4-16 (Remarks, page 4). The careful reading of said texts did not reveal the reference to "one or more substrates" but only to "the lux luciferase's substrate - aldehyde" (page 25, lines 2-5; page 32, lines 5-9). Thus, the examiner is unable to locate adequate support in the specification for "one or more substrates". Therefore, there is no indication that "one or more substrates"as opposed to a single substrate, aldehyde, were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

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Claims 1-3, 5-8, 21, 22, 24-28, 34-36, 49, 56, 58, 64 and 68-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5-8, 21, 22, 24-28, 34-36, 49, 56, 58, 64 and 68-82 comprise polynucleotides encoding "*lux*" genes. The specification defines "*lux*" genes as "prokaryotic genes associated with luciferase and photon emission" (page 18, lines 22-23). Thus, a genus of any "*lux*" gene encompasses both naturally occurring in any prokaryote wherein the *lux* operon has any order of the genes and man made or mutated genes.

The specification teaches the *lux* operon of *Photorhabdus* (*Xenorhabdus*) *luminescens* wherein the genes in the *lux* operon are ordered *luxCDABE*. The specification and the art teach that eleven species in four Gram-negative genera are known (page 1, lines 10-13). The claims are not limited to the *lux* genes from Gram-negative bacteria homologous to *lux* genes from *Photorhabdus luminescens* wherein the genes in the *lux* operon are ordered *luxCDABE*. The specification does not contain any disclosure of the structure and function of DNA sequences that encode *lux* polypeptides from other prokaryotic organisms. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding

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many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus, a DNA encoding *lux* gene products from Gram-negative bacterium *Photorhabdus luminescens*. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of encoding a *lux* polypeptide and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 25-27, 35 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 6-8 and 25-27 recite "Sa1", "Sa2", "Sa3", "Sa4", "Sa5", "Sa6", "Sp1", "Sp5", "Sp6", "Sp9", "Sp16" and "Sp17". The metes and bounds of these abbreviations are not defined in the specification.

Claims 35 and 71 recite "mini-transposon". The metes and bounds of this term are not defined in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8, 49, 56, 58, 64 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meighen in view of Vellanoweth et al.

Meighen et al. (form PTO-1449 filed October 16, 2001, reference AR-1) teach organization and function of the *lux* genes in Gram-negative bacteria and their expression in Gram-negative bacteria. They teach that in the *lux* operon the luciferase genes (*luxAB*) are flanked by genes involved in synthesis of its fatty aldehyde substrate (*luxCDE*) (page 122). Transcription of the *lux* operon results in a polycistronic RNA encoding all gene products.

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Vellanoweth et al. teach the importance of the Shine-Dalgarno (S/D) sequence for the translation in both Gram-negative *Escherichia coli* and Gram-positive *Bacillus subtilis*. They teach the effect of S/D sequence on the translation of *E. coli* β -galactosidase in *B. subtilis*. They disclose S/D sequences that allow the best translation in *B. subtilis* (page 1107, Table 1 and Figure 2). These S/D sequences comprise SEQ ID NO: 1 of the instant invention as required by claim 3. With regard to claim 49, they teach a shuttle vector comprising cassette comprising DNA encoding β -galactosidase, a selectable marker and both Gram-positive and Gram-negative origin of replication (page 1111, 2nd column, through page 1112, 1st column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Gram-positive ribosome binding site (RBS) comprising S/D sequences taught by Vellanoweth et al. in cassettes comprising the entire *lux* operon and intended for transforming Gram-positive bacteria. The RBS must be located 5' to all of the *lux* genes to ensure the translation of all of the *lux* genes. It would have been obvious to use various control, or regulatory, sequences, such as promoters that have been available in the art at the time the invention was made to modify the expression of the *lux* genes. One of ordinary skill in the art would have been motivated to express a useful *lux* reporter instead of β -galactosidase reporter in *B. subtilis* in view of it convenience taught by Meghen et al. One of ordinary skill in the art would be motivated to express a *lux* reporter in any Gram-positive bacteria that has been known to have

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an industrial or medicinal importance. One of ordinary skill in the art would have a high expectation of success because the means for transforming gram-positive bacteria with genes from Gram-negative bacteria were available in the art at the time the invention was made and are taught by Vellanoweth et al.

Claims 6-8 are included in this rejection because absent the definition, the recited sequences have been construed as any promoter/enhancer sequences.

Claims 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meighen in view of Vellanoweth et al. and further in view of Legocki et al.

The teachings of Meighen and Vellanoweth et al. are outlined above.

Legocki et al. (US Patent 5,221,623) teach a transposon, mini-Mu lux, obtained by insertion the *Vibrio harveyi lux* AB genes disconnected from their native promoter into the transposon mini-Mu (column 1, lines 18-68). They teach that mini-Mu lux can be inserted into a target gene producing light as a function of target gene transcription (column 2, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to insert Gram-positive RBS 5' to all the *lux* genes in mini-Mu lux transposon taught by Legocki et al. in order to make a transposon effective for transforming Gram-positive bacteria.

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Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meighen in view of Vellanoweth et al. and further in view of Sherf et al.

The teachings of Meighen and Vellanoweth et al. are outlined above.

Sherf et al. (US Patent 5,670,356) teach the use of a modified form of beetle luciferase gene where the DNA sequence was modified using codons more common in mammals in order to improve the expression of beetle luciferase *luc* reporter gene in mammalian cells (column 9, line 19, through column 10, line 7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize codons of the *lux* genes in accordance with the codon preference of a host cell similarly to the teachings of Sherf et al.

Allowable Subject Matter

Claim 29 is objected to as being dependent upon a rejected and objected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed November 13, 2002 have been fully considered but they are not persuasive.

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With regard to the written description rejection, Applicants argue that "To date, at least eleven species in four Gram-negative genera have been described ... In all these species, the five genes responsible for bioluminescence are clustered in the *lux* operon (*luxCDABE*)" *Remarks, page 7). This is not persuasive because the claims are not drawn to the *lux* genes from the Gram-negative bacteria wherein they are ordered CDABE in the *lux* operon. They are drawn to *lux* genes that are defined in the specification as "prokaryotic genes associated with luciferase and photon emission", i.e., to any prokaryotic luciferase genes (page 18, lines 22-24).

Applicants further argue that they "set forth structure: function characteristic (i.e., "the luciferase enzyme is encoded by two subunits (*luxAB*)" and "the fatty acid reductase polypeptides responsible for the biosynthesis of the aldehyde substrate for the luminescent reaction are encoded by the three genes *luxCDE*") (page 8). This is not persuasive because such limitations are absent from the claims and the claims in fact are directed to any prokaryotic luciferase genes.

With regard to the 103(a) rejections, the examiner addressed the outstanding issues in the reworded and/or newly applied rejections.

The examiner clarifies that claim 83 is withdrawn.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is

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(703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD
Primary Examiner

February 7, 2003